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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
BELYAVSKYI, MICHAIL A	

ART UNIT	PAPER NUMBER
1644	11

DATE MAILED: 06/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/988,971	CHANG ET AL.	
	Examiner	Art Unit	
	Michail A Belyavskyi	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 March 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *8* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicant's amendment, filed 3/11/03 (Paper No. 10), is acknowledged.

Claims 21-40 are pending.

2. Applicant's election without traverse of Group I, claims 1-7, 13 17 and 18 (now claims 21-40) in Paper No. 10 is acknowledged.

Claims 21-40 are under consideration in the instant application.

3. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention *to which the claims are directed.*

4. Applicant's IDS, filed 08/5/02 (Paper No. 8), is acknowledged. The AF citation has been crossed out. Applicant is required to provide the date and page numbers for said citation. ALL REFERENCES SHOULD BE DATED AND HAVE PAGE NOS.

5. The disclosure is objected to because of the following informalities: on page 24, lines 14-15 the date of Deposit and ATCC Accession Number for hSLAP-2 cDNA are missing.

Appropriate correction is required.

6. 35 U.S.C. § 101 reads as follows:

"Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

7. Claims 21-40 are rejected under 35 U.S.C. 101 as the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility.

Applicant is directed to the Revised Interim Utility Guidelines, Federal Register, Vol. 64, No. 244, pages 71427-71440, Tuesday December 21, 1999. In keeping with the revised utility guidelines and corresponding training materials (available on the PTO Website), none of the disclosed uses is a specific, and/or substantial use.

The specification disclosed a novel nucleic acid molecules of SEQ ID NO: 1 encoding SH2/SH3 domain –containing protein h SLAP-2 of SEQ ID NO:2. The specification fails to provide sufficient objective evidence of any activity for encoded protein. Applicant only states that said protein shows 47 % identity to human SLAP and 58 % identity to the mouse SLAP proteins (see Table 4 and page 61, lines 22-30 in particular). The specification disclosed that based on sequence homology to related molecules , said protein may be a novel human SLAP-2 protein. The specification also disclosed that said hSLAP-2 nucleic acid sequence and related protein can be used for diagnosing, treating or preventing disorders or diseases associated with aberrant or uncontrolled cellular signal transduction or with hyperactive cell, or may play a role in one or more aspects of regulating the immune system and tumor cell biology (see page 20, lines 5-20 and page 41, lines 22-30 in particular). No well-established utility for a human SLAP-2 protein is indicated.

There is no information pertaining to the significance of the percentage homology, e.g. whether there were any conserved motifs that would led the artisan to accept the protein's function. Moreover, neither the specification nor the prior art disclose any information regarding the evolutionary significance of this homology or relative conservation of structure and function across species. For example, there is no evidence of record showing why homology to a mouse SLAP would provide a better basis for assigning protein function than homology to a human SLAP . Identifying a protein as having a limited homology to said proteins does not indicate what function it might have. No well-established utility for a h SLAP-2 of SEQ ID NO:2 is indicated. Moreover, Holland et al., (J. Exp. Med. 2001, Vol.14, 1263-1276) teach that although SLAP-2 and SLAP share structural homologies their mechanisms of action is different and further studies are required to determine the role and function of SLAP-2 protein (see overlapping pages 1273 –1274 in particular).

After further research, specific and substantial utility might be found for claimed polypeptide h SLAP-2 of SEQ ID NO:2. This further characterization, however is part of the act of invention and until it has been undertaken, Applicant's claimed invention is incomplete. A well-established utility is a specific, substantial, and utility that is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material.

In support, Skolnick et al. (Trends in Biotech., 18(1):34-39, 2000) disclose that the skilled artisan is well aware that assigning functional activities for any particular protein or protein family based upon sequence homology is inaccurate, in part because of the multifunctional nature of proteins (e.g., "Abstract" and "Sequence-based approaches to function prediction", page 34).

Even in situations where there is some confidence of a similar overall structure between two proteins, only experimental research can confirm the artisan's best guess as to the function of the structurally related protein (see in particular "Abstract" and Box 2). Attwood *et al.* (Science, 2000, 290, 471-473) teach that protein function is context-dependent and the state of the art of making functional assignments merely on the basis of some degree of similarity between sequences and the current structure prediction methods is unreliable. Given the above information, and in light of the art recognized fact that minor sequence differences can significantly affect a protein's function, one skilled in the art would find it more likely than not that h SLAP-2 of SEQ ID NO:2 is not having the same function as human SLAP. Thus, the homology-based assignment h SLAP-2 of SEQ ID NO:2 as human SLAP receptor does not appear to provide evidence of a specific and substantial utility based on the knowledge of the skilled artisan and the data presented in the instant specification.

There is no specific disease or specific function that is suggested by this limited homology. There is therefore no specific or substantial, utility that is well-known, apparent, or implied by the relationship of the instant polynucleotide to the polynucleotide encoding by human SLAP or mouse SLAP.

A utility such as chromosome localization would apply to virtually every naturally occurring polynucleotide and is therefore not specific. Likewise, tissue-specific expression does not rely on specific properties or functions of the encoded protein. Each nucleic acid sequence that is expressed within a multicellular organism is expressed in some cell type and this expression is regulated in either a temporal or spatial manner. That, is, each expressed sequence is expressed in some cell type at some point in a hosts lifetime. Some transcripts are expressed embryonically, others are expressed only in particular cells, while still others are expressed in a wide variety of cells. In addition, some transcripts which are expressed in particular cells are only expressed in response to certain metabolic or environmental stimuli. Therefore, mere expression does not appear to provide evidence of a specific and substantial utility based on the knowledge of the skilled artisan and the data presented in the instant specification.

Further, the specification does not disclose any diseases or conditions known to be associated with the hSLAP polypeptide , encoded by SEQ ID NO:2 or any conditions associated with altered levels (increase or decrease) of said polypeptide. Since any protein may potentially be used as a treatment agent, this utility would not be considered to be specific. Since no particular disease or condition is disclosed, the artisan would have been required to perform additional experimentation to identify and/or reasonably confirm the asserted use of hSLAP polypeptide as a treatment agent and therefore, this utility would not be considered to be substantial. Therefore, identification of hSLAP polypeptide , encoded by SEQ ID NO:2 or nucleic acid of SEQ ID NO:1, encoding said polypeptide would not be sufficient to identify or confirm a "real world" context of use; clearly further research would be required to identify a disease in which the encoded protein is involved that can be treated using said a protein or nucleic acid encoding said protein .

Thus, the disclosed utilities do not appear to be either specific or substantial because the specification fails to disclose a specific and substantial utility for either the nucleic acid of SEQ ID NO:1 or the polypeptide having the amino acid sequence of SEQ ID NO:2. Therefore, (1) An isolated nucleic acid molecule, comprising a polynucleotide sequence selected from the group recited in claim 21; or , 2) the isolated polynucleotide of claim 21 wherein said nucleotide sequence further comprises a heterologous nucleic acid sequence, claimed in Claim 36; or 3) an isolated nucleic acid molecule comprising a polypeptide having a nucleotide sequence at least 85% identical to a sequence provided in claim 21, claimed in claim 38 or further comprising a heterologous nucleic acid sequence, as claime in Claim 39 and 40 each appear to constitute research reagents for further experimentation to discover a "real world " utility for the claimed invention.

Thus, for the above mentioned reasons there does not appear to be either a specific and substantial asserted utility, or a well-established utility for the claimed (1) An isolated nucleic acid molecule, comprising a polynucleotide sequence selected from the group recited in claim 21; or , 2) the isolated polynucleotide of claim 21 wherein said nucleotide sequence further comprises a heterologous nucleic acid sequence, claimed in Claim 36; or 3) an isolated nucleic acid molecule comprising a polypeptide having a nucleotide sequence at least 85% identical to a sequence provided in claim 21, claimed in claim 38 or further comprising a heterologous nucleic acid seqence, as claime in Claim 39 and 40 .

In addition, since polynucleotide comprises SEQ ID NO:1 and protein , encoded by SEQ ID NO:2 itself appears to constitute a research reagent, recombinant vectors , host cells comprising SEQ ID NO:1 or related sequences and methods of making an isolated polypeptide comprising said sequences also do not appear to have a specific and substantial utility, or a well established utility.

Applicant is directed to the Utility Examination Guidelines, Federal Register, Vol. 66, No. 4, pages 1092-1099, Friday January 5, 2001.

As such, further research would be required. See Brenner v. Manson, 383 U.S. 519, 535-36, 148 USPQ 689, 696 (1966), the court indicates "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion." A patent is therefore not a license to experiment. Because the claimed invention is not supported by a specific asserted utility for the reasons set forth, credibility of any utility cannot be assessed.

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 21-40 also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial, asserted utility or a well established utility for the reasons set forth in the rejection under 35 USC101 above, one skilled in the art clearly would not know how to use the claimed invention.

10. Claims 21 and 26-40 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention.

The specification does not reasonably provide enablement for: (i) *any* isolated nucleic acid molecule, comprising a polynucleotide sequence selected from the group recited in claim 21 (c-h), claimed in claims 21 (c-h) 26 and 28 -32 ; or (ii) *any* isolated nucleic acid molecule, comprises nucleotide 694 to 942 of SEQ ID NO:1, claimed in claim 27; or (iii) *any* recombinant vector comprising any polynucleotide sequence selected from the group recited in claim 21 (c-h), or any recombinant host cells comprising said vectors , or a method of making any isolated polypeptide, comprising culturing said recombinant host cells claimed in claims 33 , 34 and 35 accordingly; or (iv) *any* isolated polynucleotide of claim 21 wherein said nucleotide sequence further comprises a heterologous nucleic acid sequence, claimed in Claims 36 and 37; or (v) *any* isolated nucleic acid molecule comprising a polypeptide having a nucleotide sequence at least 85% identical to a sequence provided in claim 21, claimed in claim 38 or further comprising a heterologous nucleic acid sequenced, claimed in Claim 39 and 40 .

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification does not enable one of skill in the art to practice the invention as claimed without undue experimentation.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the limited working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention.

The claims as written encompass the genus of nucleic acid sequences. The genus encompasses nucleic acid sequences wherein such nucleic acid have numerous differences in nucleic acid sequences.

Applicant discloses an isolated nucleic acid sequence of SEQ ID NO:1, encoding the full length hSLAP-2 polypeptide of SEQ ID NO:2 and complement thereof in the instant specification. Applicant has not taught how to make and/or use : (i) *any* isolated nucleic acid molecule, comprising a polynucleotide sequence selected from the group recited in claim 21 (c-h), claimed in claims 21 (c-h) 26 and 28 -32 ; or (ii) *any* isolated nucleic acid molecule, comprises nucleotide 694 to 942 of SEQ ID NO:1, claimed in claim 27; or (iii) *any* recombinant vector comprising_any polynucleotide sequence selected from the group recited in claim 21 (c-h), or any recombinant host cells comprising said vectors , or a method of making any isolated polypeptide, comprising culturing said recombinant host cells claimed in claims 33 , 34 and 35 accordingly; or (iv) *any* isolated polynucleotide of claim 21 wherein said nucleotide sequence further comprises a heterologous nucleic acid sequence, claimed in Claims 36 and 37; or (v) *any* isolated nucleic acid molecule comprising a polypeptide having a nucleotide sequence at least 85% identical to a sequence provided in claim 21, claimed in claim 38 or further comprising a heterologous nucleic acid sequenced, claimed in Claim 39 and 40 . The structural and functional characteristics of said nucleic acid molecules are not defined in the claim.

"Comprising" is considered open-ended claim language and expand an isolated nucleic acid molecule to include additional non disclosed nucleic acids sequences outside of the specified sequences. The disclosure of SEQ ID NOS: 1 cannot support the entire genus of (i) *any* isolated nucleic acid molecule, comprising a polynucleotide sequence selected from the group recited in claim 21 (c-h), claimed in claims 21 (c-h) 26 and 28 -32 ; or (ii) *any* isolated nucleic acid molecule, comprises nucleotide 694 to 942 of SEQ ID NO:1, claimed in claim 27; or (iii) *any* recombinant vector comprising_any polynucleotide sequence selected from the group recited in claim 21 (c-h), or any recombinant host cells comprising said vectors , or a method of making any isolated polypeptide, comprising culturing said recombinant host cells claimed in claims 33 , 34 and 35 accordingly; or (iv) *any* isolated polynucleotide of claim 21 wherein said nucleotide sequence further comprises a heterologous nucleic acid sequence, claimed in Claims 36 and 37; or (v) *any* isolated nucleic acid molecule comprising a polypeptide having a nucleotide sequence at least 85% identical to a sequence provided in claim 21, claimed in claim 38 or further comprising a heterologous nucleic acid sequenced, claimed in Claim 39 and 40.

There does not appear to be sufficient guidance in the specification as filed as to how the skilled artisan would make the various nucleic acids recited in the instant claims. A person of skill in the art would not know which sequences are essential and which sequences are non-essential. There is insufficient guidance to direct a person of skill in the art to select particular sequences or sequence lengths as essential for the function of nucleic acid sequence of SEQ ID NO:1 and polypeptide encoded by the amino acid sequence of SEQ ID NO: 2. Moreover, there is insufficient guidance as to which "isolated polynucleotide comprising a heterologous polynucleotide", recited in the claims 36 and 37 and which "heterologous polypeptide" recited

in claim 39-40, would maintain the same function as polypeptide encoded by amino acid sequence of SEQ ID NO: 1
Thus there appears to be insufficient guidance in the specification as filed to direct a person skill in the art to *select particular nucleotide sequence as encoding amino acids essential for the functional properties of the polypeptide. In addition, no functional properties of hSLAP-2 even disclosed.*

Applicant is relying upon certain biological activities and the disclosure of a single species to support an entire genus. It is well known that minor structural differences among even structurally related compounds or compositions can result in substantially different biology, expression, and pharmacology of proteins. Therefore, structurally unrelated (i) *any* isolated nucleic acid molecule, comprising a polynucleotide sequence selected from the group recited in claim 21 (c-h), claimed in claims 21 (c-h) 26 and 28 -32 ; or (ii) *any* isolated nucleic acid molecule, comprises nucleotide 694 to 942 of SEQ ID NO:1, claimed in claim 27; or (iii) *any* recombinant vector comprising any polynucleotide sequence selected from the group recited in claim 21 (c-h), or any recombinant host cells comprising said vectors , or a method of making any isolated polypeptide, comprising culturing said recombinant host cells claimed in claims 33 , 34 and 35 accordingly; or (iv) *any* isolated polynucleotide of claim 21 wherein said nucleotide sequence further comprises a heterologous nucleic acid sequence, claimed in Claims 36 and 37; or (v) *any* isolated nucleic acid molecule comprising a polypeptide having a nucleotide sequence at least 85% identical to a sequence provided in claim 21, claimed in claim 38 or further comprising a heterologous nucleic acid sequenced, claimed in Claim 39 and 40 as part of their sequence encompassed by the claimed invention would be expected to have greater differences in their activities.

Since the nucleic acid sequence of a polynucleotide determines its protein coding properties, predictability of which changes can be tolerated in a polynucleotide's nucleic acid sequence and still retain similar functions and properties requires a knowledge of, and guidance with regard to which nucleic acids within the full-length nucleotide sequence, if any, are tolerant of modification and which are conserved or less tolerant to modification, and detailed knowledge of the ways in which the product's structure relates to its functional usefulness. Because there is no guidance in the specification as to which amino acid sequence within the full-length amino acid sequence of SEQ ID NO: 2, which encoded hSLAP-2 that after substitution, deletion or insertion will retain the same function, it is unpredictable to determine which polynucleotide comprising a polynucleotide sequence that encodes a polynucleotide sequence that has at least "85% identity" to a sequence provided in claim 21, will have similar function. Since the structure associated with functions of any polynucleotide mentioned above are not disclosed, predicting which polynucleotide that has at least 85% identity to the nucleic acid sequence , encoding the hSLAP-2 of SEQ ID NO: 2 having the same function as amino acid sequence of SEQ ID NO: 2 is well outside the realm of routine experimentation.

As discussed supra, Attwood (Science 2000; 290:471-473) teaches that "[i]t is presumptuous to make functional assignments merely on the basis of some degree of similarity between sequences. Similarly, Skolnick et al. (Trends in Biotech. 2000; 18(1):34-39) teach that the skilled artisan is well aware that assigning functional activities for any particular protein or protein family based upon sequence homology is inaccurate, in part because of the multifunctional nature of proteins (e.g., "Abstract" and "Sequence-based approaches to function prediction", page 34). Even in situations where there is some confidence of a similar overall structure between two proteins, only experimental research can confirm the artisan's best guess as to the function of the structurally related protein (see in particular "Abstract" and Box 2). Finally, even single amino acid differences can result in drastically altered functions between two proteins. For example, Metzler et al. (Nature Structural Biol. 1997; 4:527-531) show that any of a variety of single amino acid changes can alter or abolish the ability of CTLA4 to interact with its ligands CD80 and CD86 (e.g., summarized in Table 2). Thus it is unpredictable if any functional activity will be shared by two polypeptides having less than 100% identity over the full length of their sequences.

In view of this unpredictability; the skilled artisan would not reasonably expect a polypeptide having anything less than 100% identity *over the full length of SEQ ID NO:2* to *share the same function* as the polypeptide of SEQ ID NO:2. Thus the recitation of percent identity language, in the absence of *a testable function* and limitations regarding the *sequence length over which the percent identity is required*; does not allow the skilled artisan to make and use the encoding nucleic acids commensurate in scope with the instant claims without undue experimentation.

Similarly, the fact that two nucleic acid sequences will hybridize under moderate or stringent conditions does not in and of itself require that the two sequences share any functional activity. Thus the same observations apply to the recitation of "a polynucleotide capable of hybridizing under stringent condition", claimed in claim 21 (h) as were noted above with respect to "percent identity" language. Further, it was well known in the art at the time the invention was made that hybridization could occur between two sequence based upon short stretches of 100% identity. Thus a great deal of sequence variability *with respect to the full-length nucleic acid* is possible and in the absence of a clear recitation that the identity is over the full length of SEQ ID NO:1, the claim reads on subsequences and would be viewed by the skilled artisan as been even less likely to encode a polypeptide with the same function as polypeptide encoded by SEQ ID NO:2. Finally, hybridization under conditions other than high stringency would be expected to permit a great deal of variation between the two hybridizing sequences, making it even more unpredictable that the two sequences would share the same function. Thus as for the recitation of percent identity, hybridization language in the absence of *a testable function* and limitations regarding both the *hybridization conditions* and the *sequence length over which the hybridization takes place*; does not allow the skilled artisan to make and use the hybridizing nucleic acids commensurate in scope with the instant claims without undue experimentation.

The instant Claims encompass fragments. For example, a nucleic acid comprising of a fragment of at least 100 contigous amino acid of SEQ ID NO:2, claimed in claim 21 (e); or isolated nucleic acid molecule, comprising a polynucleotide sequence selected from the group recited in claim 21 (b-d), or isolated nucleic acid molecule, comprises nucleotide 415 to 1197 of SEQ ID NO:1, claimed in claim 23; or isolated nucleic acid molecule, comprises nucleotide 517 to 684 of SEQ ID NO:1, claimed in claim 25 , or isolated nucleic acid molecule, comprises nucleotide 694 to 942 of SEQ ID NO:1, claimed in claim 27. There is insufficient guidance as to which nucleic acid residue within the nucleic acid sequence mention above or amino acid sequence within a polypeptide encoded by amino acid sequence of SEQ ID NO: 2 are *essential for the functional properties of nucleic acid molecule or the encoded polypeptide.*

Ngo *et al* teach that the amino acid positions within the polypeptide/protein that can tolerate change such as conservative substitution or no substitution, addition or deletion which are critical to maintain the protein's structure will require guidance (see Ngo *et al.*, 1994, The protein Folding Problem and Tertiary Structure Prediction, pp.492-495). Similarly, Skolnick *et al.* (Trends in Biotech., 18(1):34-39, 2000) teach that sequence-based methods for function prediction are inadequate because of the multifunctional nature of proteins (see the abstract Page 34). Such a recitation does not require that the nucleic acid encode the full length sequence set forth in SEQ ID NO:I; but rather encompasses any nucleic acid sequence comprising either the full length of SEQ ID NO:I or any contiguous nucleic acid residues. Without sufficient guidance, the changes which can be made in nucleic acid sequence of SEQ ID NO: I and still maintain activity is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

Reasonable correlation must exist between the scope of the claim and the scope of enablement set forth. Without sufficient guidance, the changes which can be made in the instantly recited nucleic acid sequences or proteins encoded by the recited nucleic acid sequences and still maintained the functional properties of SEQ ID NO: I and protein encoded by SEQ ID NO: 2 is unpredictable, as is the identity of which fragments would encode a functional polypeptide since the amino acids encoding a particular functional activity do not appear to have been identified; thus the experimentation left to those skilled in the art is unnecessary, improperly, extensive and undue.

Thus, Applicant has not provided sufficient guidance to enable one skill in the art to make and use claimed (i) *any* isolated nucleic acid molecule, comprising a polynucleotide sequence selected from the group recited in claim 21 (c-h), claimed in claims 21 (c-h) 26 and 28 -32 ; or (ii) *any* isolated nucleic acid molecule, comprises nucleotide 694 to 942 of SEQ ID NO:1, claimed in claim 27; or (iii) *any* recombinant vector comprising_any polynucleotide sequence selected from the group recited in claim 21 (c-h), or any recombinant host cells comprising said vectors , or a method of making any isolated polypeptide, comprising culturing said recombinant host cells claimed in claims 33 , 34 and 35 accordingly; or (iv) *any* isolated polynucleotide of

claim 21 wherein said nucleotide sequence further comprises a heterologous nucleic acid sequence, claimed in Claims 36 and 37; or (v) *any* isolated nucleic acid molecule comprising a polypeptide having a nucleotide sequence at least 85% identical to a sequence provided in claim 21, claimed in claim 38 or further comprising a heterologous nucleic acid sequenced, claimed in Claim 39 and 40 reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement. *In re Fisher*, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

In view of the quantity of experimentation necessary, the unpredictability of the art, the lack of sufficient guidance in the specification, the limited working examples, and the limited amount of direction provided given the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

11. Claims 21 and 26 -40 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of : An isolated polynucleotide comprising a polynucleotide sequence selected from the group recited in Claim 21 (a-b and f); an isolated polynucleotide consisting of a polynucleotide sequence selected from the group recited in Claim 21 (c-d,); isolated nucleic acid molecule, consisting of nucleotide 415 to 1197 of SEQ ID NO:1, isolated nucleic acid molecule, consisting of nucleotide 517 to 684 of SEQ ID NO:1; isolated nucleic acid molecule, consisting of nucleotide 694 to 942 of SEQ ID NO:1.

Applicant is not in possession of : (i) *any* isolated nucleic acid molecule, comprising a polynucleotide sequence selected from the group recited in claim 21 (c-h), claimed in claims 21 (c-h) 26 and 28 -32 ; or (ii) *any* isolated nucleic acid molecule, comprises nucleotide 694 to 942 of SEQ ID NO:1, claimed in claim 27; or (iii) *any* recombinant vector comprising any polynucleotide sequence selected from the group recited in claim 21 (c-h), or any recombinant host cells comprising said vectors , or a method of making any isolated polypeptide, comprising culturing said recombinant host cells claimed in claims 33 , 34 and 35 accordingly; or (iv) *any* isolated polynucleotide of claim 21 wherein said nucleotide sequence further comprises a heterologous nucleic acid sequence, claimed in Claims 36 and 37; or (v) *any* isolated nucleic acid molecule comprising a polypeptide having a nucleotide sequence at least 85% identical to a sequence provided in claim 21, claimed in claim 38 or further comprising a heterologous nucleic acid sequenced, claimed in Claim 39 and 40.

Applicant has disclosed a limited number of species; therefore, the skilled artisan cannot envision all the contemplated nucleic acid sequence possibilities recited in the instant claims. Consequently, conception in either case cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the

complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. The sequences themselves are required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993).

A description of a genus of nucleic acid sequences may be achieved by means of a recitation of a representative number of nucleic acid sequences, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. Regents of the University of California v. Eli Lilly&Co., 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

12. The following is a quotation of the second paragraph of 35 U.S.C. 112.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. Claims 21 and 32- 40 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 21 (h) is indefinite in the recitation of "a polynucleotide capable of hybridizing under stringent conditions" because the metes and bounds of such conditions are ambiguous and unclear . It is suggested that Applicant amend the claims to recite a particular set of hybridization and wash conditions to overcome this rejection.

14. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which Applicant may become aware in the specification.

15. No claim is allowed.

16. The prior art does not teach or suggest the claimed invention recited in claims 21-40

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michail Belyavskyi whose telephone number is (703) 308-4232. The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Michail Belyavskyi, Ph.D.
Patent Examiner
Technology Center 1600
June 2, 2003

Christina Chan

CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
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